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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,191	05/21/2002	Tao Chen	016303-007010US	5092

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EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT PAPER NUMBER

1615

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/674,191

Applicant(s)

CHEN ET AL.

Examiner

Gollamudi S Kishore, Ph.D

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 5,8,11,36 and 37 is/are allowed.
- 6) ☒ Claim(s) 1-4,6,7,9,10,12-35 and 38-46 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 8-15-2001.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Claims included in the prosecution are 1-46.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 15-17, 22-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term, phosphoglycerides encompasses the individual phospholipids also recited in claim 15. It is unclear as to what applicant intends to convey by 'non-cationic

lipids' recited in claim 15. This term could refer to anionic lipids and neutral lipids, which are also recited in the claim since they are not cationic lipids. Also unclear is what the term, 'alternative cationic lipids' intended to convey. Aren't alternative cationic lipids are also cationic?

The examiner suggests reciting the full name of 'ATTA' in claim 22. There is no specific definition found in the specification.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Art Unit: 1615

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Edger (5,498,420).

According to instant formula in claim 1, Y in both monomers can be hydrogen; in unit one (first monomer unit) X can be NH₂ group. This would read on a copolymer

of acrylamide and acrylic acid. When X is oxygen in the second monomer unit, the polymer would read on polyacrylic acid.

Edger teaches that copolymers of acrylamide and acrylic acid are commercially available (col. 15, lines 35-37). Edger also discloses polyacrylic acid and formulations containing liposomes these polymers (col. 7, lines 15-21). The liposomes are made of egg lecithin (examples).

5. Claims 1-2, 4, 9, 12-18, 32-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Wheatley et al (4,921,757).

Wheatley et al teach that synthetic poly (carboxylic acid, poly (alphaethylarylic acid), PEAA to effect a pH dependent release of the contents of vesicles formed from egg yolk phosphatidylcholine is known in the art as disclosed by Seki et al, "pH-triggering of phosphatidylcholine membrane properties via complexation with synthetic poly (carboxylic acid)s in a meeting in Philadelphia (1984).

Art Unit: 1615

6. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Andrianov (5,500,161).

According to instant formula in claim 1, Y in unit one can be methyl group and in unit two, a hydrogen; in unit one X can be NH₂ group. This would read on a copolymer of methacrylic acid and acrylic acid.

Andrianov teaches a copolymer of methacrylic acid and acrylic acid (col. 4, lines 3-36).

7. Claims 1, 2, 6, 9, 12-16, 19, 21, 22, 27-29, 32-35 and 38-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Zalipsky et al (5,395,619).

According to instant claim 1, Y, R₁, R₂ and R₃ have optionally substituted alkyl groups.

Zalipsky discloses liposome formulations wherein the phospholipid is attached to either polyhydroxypropylmethacrylate or polyhydroxyethyl acrylate and other acrylic acid polymers. The polymer chain contains between 20 to 150 monomer units. The liposomes contain a bilayer forming phospholipid such as phosphatidylcholine and further contain cholesterol. The liposomes are either multilamellar or unilamellar of 0.1 micron sizes. The amounts of the polymer given in molar amounts in terms of polymer-lipid conjugate appear to encompass instant amounts in terms of weight. Since Zalipsky's liposomes contain the same components as in instant invention, the burden is upon applicants to show that Zalipsky's liposomes are not pH sensitive or fusogenic (abstract, col. 3, line 65 through col. 4, line 53; col. 6, lines 3-49, col. 8, line 45 through col. 10, line 19, col. 12, lines 35-38, examples and claims).

Art Unit: 1615

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 2-3, 6, 7, 10, 27-29, 38-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wheatley et al (4,921,757 cited above).

The teachings of Wheatley et al have been discussed. In essence, wheatley teaches Wheatley et al teach that synthetic poly (carboxylic acid, poly

(alphaethylarylic

acid), PEAA to affect a pH dependent release of the contents of vesicles formed from egg yolk phosphatidylcholine is known in the art. What is unclear from the reference however, as to how many monomer units are present in the polymer and as to how much polymer is present in the liposomes. However, since the prior art composition appears to perform the same pH triggered release function, it is deemed obvious to vary the molecular weight of the polymer or its amounts to obtain the best possible results.

Wheatley does not teach that the knowledge in the art of other derivatives of PEAA derivatives wherein R2 is C 10 to C 18 alkyl. However, since homologues behave the same way, it is deemed obvious to one of ordinary skill in the art to vary the alkyl chain length in PEAA with a reasonable expectation of success. Wheatley also does not teach a method of delivery of an active agent. However, in view of since liposomes are

Art Unit: 1615

known carriers for drugs, it is reasonable to extend the pH triggered release of the contents of the art known liposomes to deliver a specific drug with a reasonable expectation of obtaining similar release.

10. Claims 19-26, 30-31 and 38-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wheatley et al (4,921,757 cited above), further in view of Woodle et al (5,013,556).

In essence, Wheatley teaches Wheatley et al teach that synthetic poly (carboxylic acid, poly (alphaethylarylic acid), PEAA to affect a pH dependent release of the contents of vesicles formed from egg yolk phosphatidylcholine is known in the art. It is unclear from Wheatley whether the liposomes contain cholesterol and polyethylene glycol. As also pointed out above, there are no explicit teachings in Wheatley whether the art known liposomes contain an active agent for subsequent delivery.

Woodle teaches that inclusion of PEG in liposomes improves their blood circulation times. The molecular weight of PEG ranges from 120 to 20,000. Woodle's liposomes further contain cholesterol from 10-40 mole percent. The liposomes are of sizes of about 0.05 microns and the method of delivery is by intravenous administration (abstract, col. 6, lines 16-17, examples and claims).

It would have been obvious to include PEG and cholesterol in instant amounts in the art known pH sensitive liposomes since such an inclusion would enhance the circulation time of the liposomes. The use of pH sensitive liposomes for the intravenous delivery of active agents would have been obvious to one of ordinary skill in the art

Art Unit: 1615

since such an administration using liposomes is known in the art as evident from Woodle.

11. Claims 1, 2, 6, 9, 12-22, 27-35 and 38-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zalipsky cited above.

As pointed out above, Zalipsky discloses liposome formulations wherein the phospholipid is attached to either polyhydroxypropylmethacrylate or polyhydroxyethyl

acrylate and other acrylic acid polymers. The polymer chain contains between 20 to 150 monomer units. The liposomes contain a bilayer forming phospholipid such as phosphatidylcholine and further contain cholesterol. The liposomes are either multilamellar or unilamellar of 0.1 micron sizes. What are lacking in Zalipsky are the specific examples using the said polymers in the preparation of liposomes. However, Zalipsky provides sufficient guidance through examples using other polymers and therefore, it would have been obvious to one of ordinary skill in the art to prepare liposomes having the claimed polymer with a reasonable expectation of success. What are also lacking in Zalipsky are the teachings of the source of the phosphatidylcholine (such as egg) and the amounts of the polymer in weight percentages. Zalipsky however, teaches the amounts of the polymer in a molar range of 1-30 % and assuming that these amounts do not correspond to instant claimed amounts, in the absence of showing the criticality, it is deemed obvious to one of ordinary skill in the art to vary the amounts based on the teachings and guidance provided by Zalipsky to obtain the best possible results. Zalipsky also does not provide specific amounts of cholesterol or

Art Unit: 1615

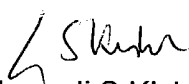
provide the source of the phosphatidylcholine (such as egg). In the absence of showing unexpected results these are deemed to be manipulatable parameters by an artisan to obtain the best possible results.

The reference of Dadey (5,935,599) is cited of interest.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615